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Mark Tengler

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EXAMINER

ANDERSON, JAMES D

ART UNIT

PAPER NUMBER

1614

DATE MAILED: 06/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/764,177

Applicant(s)

TENGLER ET AL.

Examiner

James D. Anderson

Art Unit

1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-80 is/are pending in the application.
- 4a) Of the above claim(s) 62-80 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-61 is/are rejected.
- 7) ☒ Claim(s) 2-4, 9-11, 21-23, 29-31, 42-44, and 49-51 is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|----------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>1 sheet</u> . | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Informalities

Claims 1-61 are pending and are the subject of this Office Action. Claims 62-80 are withdrawn from further consideration as being drawn to the non-elected invention (37 CFR 1.142(b)).

Priority

Acknowledgment is made of Applicant's claim of priority and benefit to U.S. Non-Provisional Application No. 10/402,858, filed March 28, 2003.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 1-61, drawn to an enveloped pharmaceutical composition comprising an immediate release first active and a sustained release second active, classified in class 514, subclass 310.
- II. Claims 62-80, drawn to a method of loading one or more actives on a bead for extended release, classified in class 424, subclass 464+, for example.

The inventions are patentably distinct and/or independent, each from the other because of the following reasons:

The inventions of Group I and Group II are related as process of making and product made. The inventions are distinct if either or both of the following can be

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shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case, the pharmaceutical composition of Group I can be made by another materially different process. For example, sustained release formulations for the sequential or timed release of medicaments are known in the art. In addition, to improve the release profile of certain sustained release dosage forms, some formulations include tablets and capsules that include a combination of an immediate release formulation and a sustained release formulation. The composition of the enveloped pharmaceutical in Group I could be made using alternate methods known in the art and does not have to be made using the method of Group II. Therefore, Groups I and II are distinct. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

Claim 1 of Group I is generic to a plurality of disclosed patentably distinct species comprising: A) gauifenesin; B) terpin hydrate; C) potassium or D) potassium guaicol sulfonate as the first active expectorant in the composition as recited in the Specification of the instant application (see especially page 14, lines 11-14). Applicant is required under 35 U.S.C. 121 to elect a single disclosed species, even though this requirement is traversed.

Should applicant traverse on the ground that the species A-D are not patentably distinct applicant should submit evidence or identify such evidence now of record

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showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Claim 1 of Group I is generic to a plurality of disclosed patentably distinct species comprising: E) decongestant; F) antihistamine; G) expectorant or H) antitussive as the second active in the composition recited in Claim 1 of the instant application. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species, even though this requirement is traversed.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

The species (Items E-H, Paragraph 4) recited in Claim 1 of Group I are each further generic to a plurality of disclosed patentably distinct species comprising the active ingredient found in a decongestant, antihistamine, expectorant, or antitussive. For example, the species decongestant (Item E) has within it a plurality of distinct active ingredients that may be selected as the second active (e.g. phenylephrine, phenylpropanolamine, and pseudoephedrine). Applicant is further required under 35

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U.S.C. 121 to elect a single disclosed active ingredient from the elected species E-H set forth in Paragraph 4, even though this requirement is traversed.

Should applicant traverse on the ground that the active ingredients of the elected species E-H are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the active ingredients to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

During a telephone conversation with Edwin Flores on April 11, 2006 a provisional election was made with traverse to prosecute the invention of Group I, Claims 1-61. In addition, a provisional election was made with traverse to prosecute the species of: a) guaifenesin as the first active expectorant and b) phenylephrine as the second active decongestant. Affirmation of this election must be made by applicant in replying to this Office action. Claims 62-80 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Notice of Possible Rejoinder

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance

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with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Claim Objections

Claims 2-3, 21-22 and 42-43 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

The claims recite the limitation “enveloped in a single dose” (Claims 2 and 21) or “enveloped into a single dose” (Claims 3 and 22). These limitations do not further limit independent Claims 1 and 20, from which the objected to claims depend, because the “enveloped pharmaceutical composition” recited in the independent claims, is inherently in a single dose. It is not clear how one would formulate an enveloped pharmaceutical composition of two actives in more than one dose.

Claims 4, 23, and 44 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

The claims recite the limitation wherein the enveloped compositions of the independent claims (Claims 1, 20, and 40) are packed into a “capsule, caplet, softgel, gelcap, suppository, film, granule, gum, insert, pastille, pellet, troche, lozenge, disk, poultrice, or wafer”. However, on page 7, lines 19-21, Applicants define the term “enveloped composition” to mean a “capsule, a suppository, a gel cap, a softgel, a lozenge, a sachet or even a fast dissolving wafer”.

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Because the independent claims are drawn to an “enveloped pharmaceutical composition”, Claims 4, 23, and 44 fail to further limit the composition to particular modes of enveloping the first and second actives since the limitations recited in these claims are already provided for by the meaning of the term “enveloped pharmaceutical” as defined by the Applicants.

Claims 9-11, 29-31, and 49-51 are objected to because of the following informalities: the word “gauifenesin” is misspelled. The correct spelling is --- guaifenesin--- as found on commercially available product labels containing this drug. Appropriate correction is required.

Claim Rejections - 35 USC § 112 – First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-61 are rejected under 35 U.S.C. 112, first paragraph, because the best mode contemplated by the inventor has not been disclosed. Evidence of concealment of the best mode is based upon the non-disclosure of the components of the “SR Mix #1” recited on Page 23, Line 29.

The instant claims are drawn to pharmaceutical compositions comprising a first active available for immediate release and a second active available for extended release. Adding a “sustained release coating” to the active, which is attached to beads

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using a pharmaceutical glaze, leads to the extended release product (Specification, Page 23, Lines 20-29). In the one example provided for formulating a sustained release second active, it is only disclosed that different levels of a sustained release coating, designated "SR Mix #1", are added. However, the components, and more specifically the particular sustained release coating, present in SR Mix #1 are not disclosed in the Specification.

The Specification only generically describes, "sustained release coatings", but does not specifically disclose what sustained release coating is appropriate or preferred in the claimed invention. Although sustained release coatings are generally known in the art, they result in different dissolution profiles depending on the specific coating's pH dependency and the thickness of the applied coating. For example, Eudragit RD100, as disclosed in the instant Specification (Page 13, Line 22), rapidly breaks down in gastric media. However, Eudragit RS 30 D is pH independent and is used in the art for sustained release formulations, whereas Eudragit L 30 D-55 is only soluble above pH 5.5 for targeted delivery to the duodenum.

Thus, the disclosure does not set forth the best mode contemplated by the inventors of formulating a sustained release composition of the second active. By not disclosing the components present in "SR Mix #1", the best mode of formulating an extended release composition of, e.g. phenylephrine, that would result in the dissolution profiles as recited in the Specification (Page 24, Table) has been effectively concealed from the public.

Claim Rejections - 35 USC § 112 – Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 60 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claim recites the limitation of a first active available for immediate effervescent release and “a second active for extended release in a mini-tab.” The claim is indefinite because it is not clear if both the first and second actives are in the mini-tab or only the second active is in the mini-tab.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claim 61 is rejected under 35 U.S.C. 102(a) as being anticipated by Davis *et al.* (U.S. Patent Application Publication No. US2003/0049318; Published March 13, 2003).

The reference teaches sustained release pharmaceutical compositions containing guaifenesin and at least one additional drug ingredient (Paragraph 17) in the form of capsules having beads or granules of both an immediate release formulation and beads or granules of sustained release formulation (Paragraph 19). The additional

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drug ingredient can be formulated within the sustained release formulation, the immediate release formulation, or both (Paragraph 20). The reference further teaches that the additional drug ingredient can be a decongestant such as phenylephrine hydrochloride (Paragraph 45).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-15, 17-19, 40-55 and 57-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Davis *et al.* (U.S. Patent Application Publication No. US2003/0049318; Published March 13, 2003) in view of Krishnamurthy *et al.* (U.S. Patent No. 6,419,960; Issued July 16, 2002) and in further view of Dang *et al.* (U.S. Patent No. 6,462,094; Issued October 8, 2002).

Davis *et al.* disclose immediate and sustained release bi-layer tablets of guaifenesin and additional drug ingredients. For example, dextromethorphan HBr was formulated into a composition for sustained release with guaifenesin (Page 14, Paragraph [0124]). In another example, pseudoephedrine (decongestant) was formulated into a composition for sustained release with guaifenesin (Page 15, Paragraph [0132]). The reference further discloses that the modified release products contain a first quantity of guaifenesin for immediate release and a second portion

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comprising a second quantity of guaifenesin and at least one additional drug ingredient in a sustained release form (Page 17, Claim 29). Guaifenesin is provided in an amount of 211 mg as, for example, in instant Claims 11, 31, and 51 in the bi-layer tablets disclosed (Page 12, Example 5). The formulations disclosed in the reference do not comprise enveloped compositions wherein the actives are disposed on separate carriers as recited in the instant claims.

Krishnamurthy *et al.* disclose modified/controlled release drug formulations and methods of making the same wherein the formulations are designed to provide a rapid initial onset of effect and a prolonged duration of effect (Abstract) as instantly claimed. The reference also discloses pharmaceutical formulations composed of a mixture of immediate release particles (*e.g.* beads) and controlled release particles (*e.g.* beads). The mixture of particles possessing different release properties are blended together and filled into hard gelatin capsules (*i.e.* "enveloped composition") as instantly claimed (see especially Column 5, Lines 20-29). The drugs used in the formulations of the disclosed invention can be selected from a "wide variety of pharmaceutically active drugs" including the instantly claimed antitussives and decongestants (Column 6, Lines 57-65). The examples of the reference disclose that the immediate release beads provide over 90% of the active within 45 minutes (Column 16, Table 2) and a formulation of controlled-release beads (second active) provides 90% of the active within 6 hours as instantly claimed (Column 18, Table 6). Different release profiles of the active ingredient can be attained by modifying the amount of coating on the beads as exemplified in the Examples provided in the reference. The immediate release

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active (*i.e.* "first active") can be superimposed on the sustained-release active (*i.e.* "second active") as instantly claimed in Claims 17, 37, and 57 (see for example Column 5, Lines 30-59) or provided in powder form in the formulation as instantly claimed in Claims 10, 30, and 50 (see especially Column 15, Lines 48-55). The formulations disclosed can also contain other inactive ingredients as instantly claimed in Claims 18, 38, and 58 (see Examples).

To the skilled artisan, the claimed subject matter as a whole would have been *prima facie* obvious at the time the invention was made because as noted above, immediate release guaifenesin tablets and bi-layer formulations of guaifenesin for immediate and sustained release, wherein the sustained release portion can contain a second drug were known in the art. In addition, the disclosures of the '960 patent provide for pharmaceutical formulations comprising both an immediate and controlled (*i.e.* extended or sustained) release of active, in enveloped compositions, wherein the immediate and controlled-release ingredients are disposed on separate carriers (*e.g.* beads). In view of the disclosures of the combined references, one of ordinary skill in the art at the time the invention was made would have appreciated that the formulations disclosed in the '960 patent could be modified to contain guaifenesin for immediate release and phenylephrine for sustained release.

One of ordinary skill would have been motivated to formulate a guaifenesin/phenylephrine formulation for immediate release of guaifenesin and sustained release of phenylephrine in view of the disclosure of Dang *et al.* who state that a combination of phenylephrine tannate and guaifenesin produces a composition

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possessing "sympathomimetic decongestant and expectorant properties superior to the use of either one of the compounds alone" (Col. 2, Lines 1-3). The reference further states that the combination of guaifenesin and phenylephrine tannate is designed to provide immediate expectorant action (guaifenesin) and prolonged decongestant action (phenylephrine) (Col. 2, Lines 11-14). One of ordinary skill in the art would appreciate that allowing guaifenesin to act as an expectorant (immediate release) prior to the decongestant action of phenylephrine (extended release) would provide the maximum benefit of both drugs. The artisan would have been imbued with at least a reasonable expectation that a composition comprising guaifenesin for immediate release and phenylephrine for extended release would provide the requisite effect desired of such a formulation.

Thus, for the above reasons, Claims 1-15, 17-19, 40-55, and 57-59 are rejected under U.S.C. 103 as being *prima facie* obvious to one of ordinary skill at the time the invention was made.

Claims 20-35 and 37-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Davis *et al.*, Krishnamurthy *et al.*, and Dang *et al.* as applied to Claims 1-15, 17-19, 40-55 and 57-59 above, and further in view of Entex® LA prescribing information (12/2002).

Davis *et al.*, Krishnamurthy *et al.*, and Dang *et al.* disclose as above. The Entex® LA prescribing information teaches that expectorants (e.g. guaifenesin) and

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decongestants (e.g. pseudoephedrine HCl) are available in formulations to relieve nasal congestion.

It would have been obvious to one of ordinary skill in the art at the time the invention was made that immediate release of an expectorant would effect physiological results (*i.e.* loosen phlegm and thin bronchial secretions) that would improve the physiological action (*i.e.* sinus drainage) of an extended release decongestant. One would be motivated to combine guaifenesin and phenylephrine because as a result of the combined actions of the expectorant and decongestant, sinus and bronchial drainage would be improved, and dry, nonproductive coughs will be more productive as disclosed in the Entex[®] LA prescribing information.

Conclusion

No Claims are allowed.

Claims 16, 36, 56, and 60 are free of the prior art of record.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James D. Anderson whose telephone number is 571-272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



James D. Anderson
Examiner
Art Unit 1614

May 18, 2006



ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER